IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of: Heath et al	Group Art Unit:1634 Examiner: Goldberg, J.
Serial No.: 09/241,636	Conf. 8977
Filed: February 2, 1999	
For: Process for Isolating, Amplifying and Characterizing DNA	

DECLARATION UNDER 37 CFR 1.132

Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Dirk Loeffert, do hereby declare as follows:

1. I obtained a PhD degree in Biology from the University of Cologne, Germany in 1996. Since then, I have worked in the field of molecular biology for more than 13 years specializing in molecular biology techniques and enzymes used for modification and amplification of nucleic acids. I have worked for Qiagen GmbH since 1996. My present title is Senior Director Research North America and Senior Director R&D Modification / Amplification.

2. I am familiar with the above-identified patent application ("the '636 application"). I am also familiar with certain prior art references being applied by the USPTO in connection with the '636 application. Due to my significant experience in the field of molecular biology techniques, I was familiar with the state of the art in 1999 when the '636 application was filed. I have become familiar with the GENERATION products

that are marketed by my employer Qiagen GmbH, and which products I understand are related to the '636 application.

3. It is my understanding that the '636 application covers lysis of a biological material that contains DNA with a solid support having dried thereon, a lysing reagent and a RNA digesting enzyme, wherein the lysing reagent includes only a detergent, optionally water, optionally a buffer and optionally a chelating agent. As one of ordinary skill in the art, I would not have expected such a system to work. That is, when I first heard of this type of assay, I did not think such an assay would work. Therefore, as one of skill in the art, to me it was completely unexpected that when a lysing reagent and an RNA digesting enzyme are dried on a support, the resultant could even be used to accomplish lysis while maintaining the RNAse enzyme activity. It is well known in the art that detergents like SDS efficiently denature proteins and thus destroy an enzyme capability to perform its function. It was even more unexpected to me that indeed the process works much faster and more efficiently than other methods for lysis of biological samples.

4. Based on literature such as, A Laboratory Guide to RNA, by Paul A. Krieg, copyright 1996, and which was available before the priority of the '636 application, it was certainly thought in the art in 1999 that a detergent would inhibit RNase (i.e. an RNA digesting enzyme). See, *i.e.* p. 76 of Dr. Krieg's book where it is stated at (i) that "SDS is an efficient anti-RNase detergent." This was my opinion as well since I believed that detergents would routinely inhibit enzymes such as RNA digestion enzymes. As one of skill in the art in 1999, I would have believed that a detergent could inactivate the RNA digesting enzyme. But surprisingly and unexpectedly by having both of these agents dried on the support together, their activity can be maintained over long term storage, and yet even more surprisingly, they are both immediately available and active upon contact of the biological sample when it is added to the support.

5. The fact products of the present application have at least similar or even superior properties to products where a lysing reagent and RNA digesting enzyme are not dried on a support, was surprising and unexpected to me, especially in view of literature such as Dr. Krieg's handbook. The fact that the specific lysing reagent (including detergent, optionally water, optionally chelating agent, optionally buffer) and an RNA digesting enzyme are dried on the support ahead of time is critical to the unexpected results. Moreover, I expect that lysis using such a support with lysing reagent and RNA digesting enzyme to work across all embodiments of the '636 application.

6. I further declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true, and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and may jeopardize the validity of the application or any patent issued thereon.

08-25-2009

Date

Dirk Loeffert, PhD